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Attn: TSCA Docket Clerk

Re: For Your Information Submission:

The enclosed information is submitted on behalf of Dow Corning Corporation, Midland, Michigan, 48686-0994, on a For-Your-Information (FYI) basis as a follow-up to submissions made concerning hexamethyldisiloxane (HMDS), which chemical substance was the subject of a health and safety data rule issued under Section 8(d) of the Toxic Substances Control Act (TSCA) and with an effective date of June 14, 1993 (sunset date June 30, 1998), as codified at 40 CFR 716 (Health and Safety Data Reporting). The information presented in this submission was generated as part of our Siloxane Research Program. This program was the subject of a memorandum of understanding, dated April 9, 1996, between Dow Corning and EPA.

Listed Chemical Substance:

107-46-0 Hexamethyldisiloxane (HMDS)

Final Study Report:

Non-Regulated Study: A One-Week Vapor Inhalation Study to Evaluate by Immunohistochemistry the Effect of Hexamethyldisiloxane (HMDS) on Alpha $_{2u}$-Globulin Accumulation in the Kidneys of Male Fischer 344 Rats

Dow Corning Corporation
2002-I0000-51723
January 22, 2003

Dow Corning Corporation
Midland, Michigan 48686-0994
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Manufacturer:

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For purposes of this TSCA For-Your-Information (FYI) submission, the general INTERNAL designation on the attached health and safety report is waived by Dow Corning.

If you require further information regarding this submission, please contact Michael Thelen, Manager of U.S. EPA Regulatory Affairs, at 989-496-4168 or at the address provided herein.

Sincerely,

Kathleen P. Plotzke
Director, Health and Environmental Sciences
(989) 496-8046

MR 269927

DOW CORNING CORPORATION
NON-REGULATED TECHNICAL REPORT

Report Number:	2002-I0000-51723
Title:	Non-Regulated Study: A One-Week Vapor Inhalation Study to Evaluate by Immunohistochemistry the Effect of Hexamethyldisiloxane (HMDS) on Alpha $_{2u}$-Globulin Accumulation in the Kidneys of Male Fischer 344 Rats
Study Number:	9620
Test Article:	Hexamethyldisiloxane (HMDS)
Study Leader:	James W. Crissman, D.V.M., Ph.D., D.A.C.V.P.
Sponsor:	Dow Corning Corporation
HES Group Manager:	Steven D. Crofoot, M.S.
Testing Facility:	Dow Corning Corporation Health and Environmental Sciences, Toxicology 2200 W. Salzburg Road Auburn, MI 48611
Study Completion Date:	January 22, 2003

GLP Compliance Statement: The work described in this report was carried out using the best available scientific methodology, and procedures were followed to assure accurate, high quality results. However, this non-regulated study was ***not*** conducted to meet all of the requirements described in Good Laboratory Practices Regulations such as those documented in the Federal Register 40 CFR Part 792.

Dow Corning Internal Information:

This report may be reproduced and shared with any Dow Corning employee. The issuing department must approve distribution outside the corporation. When this INTERNAL report is no longer needed, it may be placed in office wastebaskets for destruction.

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ABSTRACT

This non-regulated study was designed to test the hypothesis that the alpha 2u-globulin (α2u-globulin) mechanism was responsible for the nephropathy and kidney neoplasia observed in male rats on previous studies with hexamethyldisiloxane (HMDS). Seven male Fischer 344 rats per group were exposed via a nose-only vapor inhalation system to HMDS vapors at 5000 ppm or to air for 6 hrs/day for 6 days. All animals were necropsied the morning after the last exposure. Under a surgical plane of anesthesia, their kidneys were perfused with 1% glutaraldehyde and 2% paraformaldehyde. Five control and five HMDS-exposed rats had adequate renal perfusion fixation at necropsy; kidney slides were made only from these rats for light microscopy. Tissues were embedded in methyl methacrylate, and duplicate slides stained either immunohistochemically using a mouse monoclonal antibody against α2u-globulin or with Lee's methylene blue/basic fuchsin. There were HMDS exposure-induced renal effects characteristic of α2u-globulin nephropathy. HMDS exposure clearly increased the amount and altered the morphology of α2u-globulin stained material. Quantitatively, both the proportional area and density of positively stained material in the renal cortex was increased in exposed rats. Morphologically, in control rats, the α2u-globulin stained material generally had a fine stippled appearance in tubular epithelial cells, in contrast to the kidneys of HMDS-exposed rats in which the α2u-globulin stained material was more often in larger droplets or needle- or rhomboid-shaped crystals. Further, occasional tubules in α2u-globulin accumulation areas of HMDS-exposed rats showed sloughing of necrotic epithelial cells into the tubular lumen, and consequent thinning of the epithelial lining. The results provided mechanistic support for the hypothesis and it was concluded that HMDS nose-only vapor exposure at 5000 ppm for 6 hrs/day for six days caused α2u-globulin nephropathy in male Fischer 344 rats.

APPROVAL SIGNATURES

This report consists of pages 1-31 including Tables 1-2 and Appendices 1-2

Approved By:

1/22/03

James W. Crissman, D.V.M., Ph.D., D.A.C.V.P. Date
Study Leader

1/22/2003

Steven D. Crofoot, M.S, Date
Team Leader, Toxicology

STUDY INFORMATION

Experimental Start Date:	October 16, 2001
In-Life Experimental Termination Date:	November 7, 2001
Study Completion Date:	June 26, 2002
Study Leader:	James W. Crissman,
Study Coordinator:	Jane M. Regan, MLT/HT

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OBJECTIVE

The study was designed to determine whether the α2u-globulin mechanism is responsible for the observed nephropathy and kidney neoplasia observed in male rats on previous studies, and to help meet the requirements outlined by the United States Environmental Protection Agency (USEPA) (Baetcke et al., 1991) to establish that mechanism.

PERSONNEL/FACILITIES INVOLVED IN THE STUDY

A. Sponsor
Dow Corning Corporation
2200 W. Salzburg Road
Auburn, MI 48611

B. HES Group Manager
Steven D. Crofoot, M.S.
Team Leader, Toxicology

C. Testing Facility
Health and Environmental Sciences (HES)
Dow Corning Corporation
2200 W. Salzburg Road
Auburn, MI 48611

University of North Carolina
Campus Box 7400
Rosenau Hall
Chapil Hill, NC 27599

D. Study Leader
James W. Crissman DVM, PhD, DACVP
Senior Veterinary Specialist

E. Study Coordinator
Jane M. Regan, MLT/HT (ASCP)
Technologist

TEST SYSTEM

A. Species:	*Rattus Norvegicus*
B. Strain:	Fischer 344
C. Source:	Charles River (Supplier location documented in the study records
D. Age:	10 weeks minimum at experimental start
E. Body Weight:	200 g minimum at experimental start
F. Sex and number used on study:	14 males
G. Number of groups:	2 (see section XI.C.)
H. Identification methods:	Upon receipt: Individual cage labels displaying a temporary quarantine (Q) number Permanent identification: Ear tags and individual cage labels

JUSTIFICATION FOR SELECTION OF TEST SYSTEM

Fischer 344 rats were used in the toxicity studies where the kidney effects investigated here were identified. Alpha 2u-globulin nephropathy is a male rat-specific phenomenon.

METHOD OF RANDOMIZATION

After release from quarantine, rats were assigned to test groups based on a weight stratified randomization process.

HOUSING AND MAINTENANCE

A. Animal Receipt and Quarantine

Upon receipt, Animal Resource personnel inspected each animal. All animals were judged to be in good health and suitable as test animals, and were quarantined for minimum of 7 days. During the quarantine period Animal Resource personnel observed each animal at least once daily. The attending veterinarian examined all animals before release from quarantine and documented the general state of animal health.

B. Animal Housing

Animals were individually housed in suspended wire-mesh cages during quarantine and during the course of the study until the scheduled sacrifice. The cages were elevated above Bed O'Cobs ® bedding. The cages and bedding/fecal pans were routinely cleaned, consistent with good housekeeping practices.

C. Environmental Conditions

During non-exposure periods, animals were housed in an environmentally controlled animal room (12-hour fluorescent-light/dark cycle, 64-79°F, 30-70% humidity, 10-15 air changes/hr). Temperature and humidity were recorded continuously and monitored twice a day on weekdays and once a day during weekends.

D. Basal Diet

PMI® Certified Rodent Chow #5002 was offered *ad libitum* except during exposures. The manufacturer provided results of periodic analyses of the certified feed for the presence of heavy metals and pesticides. The study leader reviewed these results to ensure that contaminants were not present in concentrations that would be expected to affect the outcome of the study. Documentation of study leader review was placed in the study file.

E. Drinking Water

Municipal water, further purified by reverse osmosis, was available *ad libitum* via the automatic watering system during non-exposure times. The water was monitored routinely and analyzed on semi-annual basis. The study leader reviewed the most recent analysis results to ensure that no contaminants were present in concentration that would be expected to interfere with the integrity of the study. Documentation of study leader review was placed in the study file.

ANIMAL WELFARE ACT COMPLIANCE

This study complies with all applicable sections of the final rules of the Animal Welfare Act regulations (9 CFR, Part 1, 2, and 3) and was approved by the Laboratory Animal Care and Use Committee (LACUC) before animals were ordered.

TEST/CONTROL/REFERENCE ARTICLE SPECIFICATIONS

Results of characterizations were reviewed by the study leader

Test Article

- Identification: Hexamethyldisiloxane (*HMDS)* (supplied as Dow Corning® OS-10)
- Lot Number AA058087

• CAS Number:	000107460
• Physical Description:	Colorless liquid
• Source:	Dow Corning Corporation 2200 W. Salzburg Road Midland, MI 48686-0994
• Chemical stability:	Chemically stable (MSDS)
• Storage Conditions:	Refrigerator (4 ± 4°C)
• Expiration Date:	May 31, 2003
• Purity:	>99.9% hexamethyldisiloxane (MDMS Lot Acceptance Require-ments)
• Solubility:	Ethanol, acetone, methanol, ethyl ether, toluene, heptane (MDMS)
• Chemical characterization:	HES Study No.9034 and TIS Report Number 1998-I0000-45047
• Archive:	Samples were not retained

EXPERIMENTAL DESIGN

A. Route and Rationale of Test Article Administration

1. Route

   Nose-only vapor exposure

2. Rationale

   Inhalation exposure was used most commonly in the studies where this kidney effect was observed.

B. Inhalation Exposure

1. Exposure Chamber

   Nose-only exposures were conducted in specially designed, polyvinyl chloride (PVC) replicas of the Cannon style flow-past nose-only exposure chamber. One chamber

was used for the control animals and one for the HMDS exposures. Chambers were operated at a slight positive pressure within a containment booth which was maintained at a slight negative pressure to prevent outward leakage of test atmosphere into the room. The chamber pressure was determined during the days prior to initiation the exposures. Using a Magnehelic® gauge to continuously monitor the chamber pressure, a minimum of one reading was recorded daily. Chamber air was supplied by a Nash compressor and filtered with a series of Balston® brand filters. Airflow through the chamber was maintained at a rate providing a minimum of 500 ml/min. to each port on the chamber. Chamber temperature (22° ± 3°C), and relative humidity (20-70%) were monitored continuously and recorded at least every 30 minutes during each exposure period. While operating at nominal conditions of airflow, temperature, relative humidity, and atmospheric concentration (±10% of target), the oxygen levels were evaluated during the days prior to initiation of exposure. Oxygen levels of 19-22% were considered acceptable. Results were recorded in the study records.

2. Test Atmosphere Generation

Test article vapor was generated using a stainless steel J-tube vapor generating system containing stainless steel beads, a fluid metering device, and a carrier gas stream (compressed air from a Nash air compressor passed through a series of Balston® brand filters). The J-tube was wrapped with heating tape and maintained at 40-60°C to promote test article vaporization into the carrier gas stream. A Fluid Metering Incorporated (FMI®) pump was used to draw test article from a reservoir for delivery into the J-tube at a rate predetermined to yield the targeted chamber concentration. The carrier gas stream was used to sweep the vapor into the chamber where it was distributed to the animals. The air/vapor mixture exiting the J-tube comprised the total airflow available to the chamber. Evaluations of vapor concentration homogeneity within the chamber were performed in the days prior to initiation of animal exposures and included a minimum of three replicate samples from an individual port at each chamber level. Homogeneity results were acceptable if the average port concentrations (3 replicates) for each level were within 10% of the nominal concentration calculated during the homogeneity evaluation.

The exposure period was six hours/day for six consecutive days. Animals were placed in restraint cones, which were then loaded onto the exposure chamber. The exposure chamber operated near the targeted exposure concentration (±10%) prior to loading the animals. The exposures start and stop times were when the animals were loaded and removed from the chamber.

3. Test Atmosphere Monitoring

The test atmosphere of each chamber was monitored during the exposure using an online gas chromatograph (GC) equipped with a Flame Ionization Detector (FID).

Prior to the first day of exposure, the GC methodology was established and documented in the study files. Sample line loss was evaluated in the days prior to initiation of the exposure. A calibration curve was constructed from at least five different concentrations of test article in air, which bracketed the expected target exposure concentration. The acceptance criteria for the calibration curve included the following:

- A coefficient of variation of ≤5% for all of the bag standard samples within a calibration level
- A linear regression analysis correlation coefficient (r^2) of ≥0.98
- A ≤10% difference between the prepared bag standard concentration and the calculated bag standard concentration derived from the linear regression equation of the calibration curve.

Instrument calibration was checked prior to each exposure by analysis of a bag standard within the range of the calibration curve. This was done by sampling the bag standard at the chamber end of the sample line. If the calculated bag standard concentration was different from the prepared bag standard concentration by >10%, the bag was sampled again, if possible. If the second sampling differed by >10% again, a new bag standard was prepared and analyzed. The calibration curve was considered acceptable for use if the second sampling or bag standard was within the 10% specification. If the second bag standard was not within the 10% specification, then the calibration curve was not used, and a new calibration curve was generated that day. The new calibration curve was used for determination of chamber test article concentration for the day of exposure.

Chamber atmospheres were sampled during each exposure period using a vacuum pump to draw chamber atmosphere through a sample line from the chamber to the GC. The flow rate for the sample line was measured in the days prior to initiation of the exposure. At the GC, sample passed through a sample loop of known volume. The contents of the sample loop were injected onto the column and analyzed a minimum of twice per hour. Upon completion of the exposure, an actual measured chamber concentration was calculated as the mean of all values from the GC analysis for that day. Adjustments to the rate of test article delivery into the J-tube were made to maintain targeted test article chamber concentrations during the exposure period. Adjustments were documented and included in the study file.

Following the exposures, nominal concentrations were determined using the following equation:

$$\text{Nominal Conc.} = \frac{\text{Amount of test article used (g)} \times 24.6 \times 10^6}{\text{Volume of air passed through chamber (L)} \times \text{Molecular weight of test article}}$$

The amount of test article used was determined by the difference between pre- and post-exposure weights of the test article reservoir (grams). Total volume of air passed through the chamber was determined using the mean chamber airflow rate during the exposure (LPM) multiplied by the duration of test article generation (minutes).

4. Exposure System Set-up

The following evaluations, calibrations, and verifications were performed prior to the first exposure and repeated as necessary to ensure accurate results: chamber homogeneity, sample line flow rate, sample line loss, bag standard stability, GC/FID conditions, equipment inventory, chamber pressure, and flow meter calibration for chamber airflow. In addition, before the first exposure, animals were acclimated to the restraint cones for four consecutive days prior to initiation of the exposure. Acclimation periods were approximately one, two, four and six hours respectively.

5. Feasibility Testing

Prior to the first exposure the exposure system was run without animals to demonstrate that all of the components were functioning correctly as a system. The data generated during these activities did not necessarily meet GLPs requirements and were not reported, but were maintained as study data.

C. Organization of Test Groups and Exposure Levels

Group ID	Number /Sex/ Group*	Treatment	Exposure level (ppm)	Exposure duration (days)
1	7 Males	Compressed and filtered air	0	6
2	7 Males	HMDS	5000	6

*Seven rats per group were allocated to ensure successful perfusion fixation of the kidneys of at least 5/group.

D. Treatment Regimen

Exposures were conducted 6 hours/day for 6 days.

E. Method of Euthanasia:

Animals were anesthetized using Xylazine/Ketamine to induce a deep surgical plane of anesthesia, followed by exsanguination from the abdominal aorta and inferior vena cava following the kidney perfusion procedure.

F. Test System Observations

1. Mortality/Morbidity/Daily Observations

All animals were observed at least once daily in their cages for mortality, morbidity, and moribundity by study personnel through the completion of the in-life phase of the study.

2. Clinical Observations

General clinical observations were made at least once a day at approximately the same time, with consideration of the peak period of anticipated effects. The condition of the animals was recorded, including changes in the skin, fur, eyes, and mucous membranes; respiratory, circulatory, autonomic and central nervous system functions; motor activity, and behavior. Findings noted at the clinical examination were recorded for individual animals. The condition of animals without signs was documented in a general comment.

G. Parameters Measured

1. Individual Body Weights

Individual body weights were recorded approximately one week prior to test article administration, at study start, and just prior to the scheduled necropsy.

2. Organ Weights

No organ weights were taken.

3. Morphologic Pathology

a. Macroscopic Examination

The kidneys were fixed by retrograde perfusion through the descending aorta with a buffered fixative of 1% glutaraldehyde and 2% paraformaldehyde. After perfusion, the kidneys were removed and placed in cold (≈4°C) vials of the same fixative for 12-24 hrs, then transferred to cold sodium phosphate buffer. From this point, the kidneys, blocks (except while sectioning), and slides were stored and processed on ice or refrigerated at approximately 4°C (Burnett et al., 1989). After

fixation and removal of the kidneys, the remaining thoracic and abdominal viscera were examined *in situ* before the carcass was discarded.

b. Microscopic Examination

Slides for microscopic examination were made from the five animals from each group that were successfully perfused. Transverse slices of each kidney were embedded in glycol methacrylate. The blocks were sectioned at 2 microns on a rotary microtome, air dried at room temperature, and then mounted on labeled, ethanol-cleaned, glass slides. Duplicate sets of unstained slides were stored at approximately 4°C until shipped in an insulated container with a cold pack to the University of North Carolina (UNC) for α2u-globulin immunohistochemical staining. After staining, the slides were handled at ambient temperature (Burnett et al., 1989). A duplicate set of slides was stained with Lee's methylene blue-basic fuchsin (LMBBF, Rowley Biochemical Institute, Danvers, MA) at Dow Corning.

Details of the α2u-globulin immuno-staining process were provided by the UNC laboratory. Briefly, the slides were incubated with a primary mouse monoclonal antibody against α2u-globulin (Bayer AG). This was linked to a secondary antibody/dextran polymer/alkaline phosphatase conjugate (Dako EnVision, Dako Corp., Carpinteria, CA), then developed with New Fuchsin Substrate (BioGenex, San Ramon, CA), counter stained with Aqua Hematoxylin (Innovex Biosciences), and the slides were coverslipped. During and after staining, the slides were handled at ambient temperature.

The immunohistochemically stained slides were returned to the Dow Corning Toxicology Laboratory for evaluation by light microscopy. Along with the LMBBF slides, they were examined with attention to the amount and morphology of the α2u-globulin immunohistologically stained material and related changes.

H. Sample Identification and Storage

All samples were identified by study and animal numbers. Upon collection of the kidneys, all samples were stored on ice or refrigerated at approximately 4°C except during processing (trimming, embedding, sectioning, and staining). The finished slides were handled at ambient temperature. Blocks remained in refrigerated storage until the study was finalized.

DATA ANALYSIS

A. Parameters to be evaluated

Light microscopic kidney morphology and estimated amount of α2u-globulin stained material were evaluated.

B. Statistical methods

The data was not analyzed statistically.

RESULTS AND DISCUSSION

Five control and five HMDS-exposed rats had adequate renal perfusion fixation at necropsy; slides were made only from these rats.

There were HMDS exposure-induced renal effects characteristic of α2u-globulin nephropathy. HMDS exposure clearly increased the amount and altered the morphology of α2u-globulin stained material. Additionally, the P2 segment of the proximal renal tubules had degenerative changes associated with the accumulated protein. Specific immunohistochemical staining for α2u-globulin identified and located the accumulated material and allowed it to be semiquantified. The finer changes in cellular and protein droplet morphology were best appreciated in the kidney sections stained with Lee's methylene blue/basic fuchsin.

In all HMDS-exposed rats, there was a clear increase over the normal accumulation of α2u-globulin observed with immunohistochemical staining. The mean grade for the amount of α2u-globulin immunological staining was 2 (slight) for controls, and 4 (marked) for exposed rats (Tables 1 and 2, Appendix 1). Both the proportional area and density of positively stained material in the renal cortex was increased. In all control rats, the α2u-globulin stained material generally had a fine stippled appearance in tubular epithelial cells. In HMDS-exposed rats, the α2u-globulin stained material was more often in large droplets or needle- or rhomboid-shaped crystals. The mean grade for altered droplet morphology was 1 (very slight) for controls, and 4 (marked) for exposed rats.

The degenerative changes in the kidneys of HMDS exposed rats were characterized by sloughing of necrotic epithelial cells into the lumen of occasional tubules in droplet accumulation areas, and consequent thinning of the epithelial lining. This change was tabulated as "cellular casts," it occurred with a calculated mean grade of 1.2 (very slight+) in exposed rats, but was not seen in controls.

CONCLUSION

The results provided mechanistic support for the hypothesis and it was concluded that HMDS nose-only vapor exposure at 5000 ppm for six days caused α2u-globulin nephropathy in male Fischer 344 rats.

ARCHIVE

The protocol, amendments, any deviations, study authorization form, raw data, correspondence, and final report, will be retained in the HES archives, Dow Corning Corporation, Midland, MI 48686-0994.

REFERENCES

Baetcke KP, Hard GC, Rodgers IS, McGaughy RE (1991). Alpha 2u-globulin: association with chemically induced renal toxicity and neoplasia in the male rat. Risk Assessment Forum, U.S. Environmental Protection Agency, EPA/625/3-91/019F.

Burnett VL, Short BG, Swenberg JA (1989). Localization of α_{2u}-globulin within protein droplets of male rat kidney: immunohistochemistry using perfusion-fixed, GMA-embedded tissue sections. J. Histochem Cytochem, 37: 813-818.

TABLE 1

Summary Table of Microscopic Findings

PATHOLOGY REPORT (DRAFT) PAGE : 2
SUMMARY TABLES PROJECT NO.: DC9620

TEST ARTICLE : HMDS
TEST SYSTEM : RAT (F344), 7 days, inhalation
SPONSOR : dow corning

PATHOL. NO.: 00003 JWC
DATE : 26-JUN-02
PathData® System V6.1a

NUMBER OF ANIMALS WITH MICROSCOPIC FINDINGS BY ORGAN/GROUP/SEX
STATUS AT NECROPSY: K0

			MALE
SEX :			
DOSE GROUP:	01	02	
NO.ANIMALS:	7	7	
KIDNEYS :	5	5	
- Cellular Casts :	-	5	
Grade 1:	-	4	
Grade 2:	-	1	
- a2u immuno staining :	5	5	
Grade 2:	5	-	
Grade 4:	-	5	
- alt droplet morphol :	5	5	
Grade 1:	5	-	
Grade 4:	-	5	

TABLE 2

Individual Microscopic Findings

PATHOLOGY REPORT (DRAFT) PAGE : 3
INDIVIDUAL ANIMAL DATA PROJECT NO.: DC9620

TEST ARTICLE : HMDS *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation *DATE* : 26-JUN-02
SPONSOR : dow corning *PathData® System V6.1a*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 01, controls

ANIMAL NUMBER :	9772 MK0	9773 MK0	9774 MK0	9775 MK0	9776 MK0	9777 MK0	9778 MK0
GENERAL OBSERVATIONS	'	'	'	'	'	'	'!
KIDNEYS	0!	+	+	+	+	+	0!
- Alpha 2u globulin immunohistological staining.	.	2.	2.	2.	2.	2.	.
- altered P2 segment protein droplet morphology.	.	1.	1.	1.	1.	1.	.

TABLE 2 (continued)

Individual Microscopic Findings

PATHOLOGY REPORT (DRAFT) PAGE : 4
INDIVIDUAL ANIMAL DATA PROJECT NO.: DC9620

TEST ARTICLE : HMDS *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation *DATE* : 26-JUN-02
SPONSOR : dow corning *PathData® System V6.1a*

TABLE OF INDIVIDUAL MICROSCOPIC FINDINGS (AOFT)
DOSE GROUP : 02, High dose

ANIMAL NUMBER :	9779 MK0	9780 MK0	9781 MK0	9782 MK0	9783 MK0	9784 MK0	9785 MK0
GENERAL OBSERVATIONS	'	'	'	'	'	'	'!
KIDNEYS	+	+	+	+	+	0!	0!
- Cellular Casts	1.	1.	2.	1.	1.	.	.
- Alpha 2u globulin immunohistological staining.	4.	4.	4.	4.	4.	.	.
- altered P2 segment protein droplet morphology.	4.	4.	4.	4.	4.	.	.

APPENDIX 1

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) PAGE : 5
INDIVIDUAL ANIMAL DATA PROJECT NO.: DC9620

TEST ARTICLE : HMDS *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation *DATE* : 26-JUN-02
SPONSOR : dow corning *PathData® System V6.1a*

ANIMAL HEADING DATA
DOSE GROUP : 01, controls

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
9772	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9773	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9774	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9775	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9776	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9777	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9778	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) PAGE : 10
INDIVIDUAL ANIMAL DATA PROJECT NO. : DC9620

TEST ARTICLE : HMDS *PATHOL. NO.* : 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation *DATE* : 26-JUN-02
SPONSOR : dow corning *PathData® System V6.1a*

ANIMAL HEADING DATA
DOSE GROUP : 02, High dose

ANIMAL NUMBER	SEX M/F	DEFINED AND FINAL STATE OF NECROPSY		TEST DAYS	FIRST AND LAST DAY UNDER TEST		DATE OF NECROPSY
9779	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9780	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9781	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9782	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9783	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9784	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01
9785	M	K0	K0	7	14-NOV-01	20-NOV-01	20-NOV-01

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) PAGE : 6
INDIVIDUAL ANIMAL DATA PROJECT NO.: DC9620

TEST ARTICLE : HMDS *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation *DATE* : 26-JUN-02
SPONSOR : dow corning *PathData® System V6.1a*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, controls MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 7 * ANIMAL NO. : 9772

* NECROPSY FINDINGS

KIDNEYS:
FAILED TO PERFUSE.
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:
Tissue not present for histologic examination

---

* STATE AT NECROPSY: KO
DAYS ON TEST : 7 * ANIMAL NO. : 9773

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Alpha 2u globulin immunohistological staining, bilateral, grade 2
-altered P2 segment protein droplet morphology, bilateral, grade 1

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) — PAGE : 7
INDIVIDUAL ANIMAL DATA — PROJECT NO.: DC9620

TEST ARTICLE : HMDS — *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation — *DATE* : 26-JUN-02
SPONSOR : dow corning — *PathData® System V6.1a*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, controls — MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 7 — * ANIMAL NO. : 9774

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Alpha 2u globulin immunohistological staining, bilateral, grade 2
-altered P2 segment protein droplet morphology, bilateral, grade 1

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* STATE AT NECROPSY: KO
DAYS ON TEST : 7 — * ANIMAL NO. : 9775

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Alpha 2u globulin immunohistological staining, bilateral, grade 2
-altered P2 segment protein droplet morphology, bilateral, grade 1

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) — PAGE : 8
INDIVIDUAL ANIMAL DATA — PROJECT NO.: DC9620

TEST ARTICLE : HMDS — *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation — *DATE* : 26-JUN-02
SPONSOR : dow corning — *PathData® System V6.1a*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, controls — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 7 — * ANIMAL NO. : 9776

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Alpha 2u globulin immunohistological staining, bilateral, grade 2
-altered P2 segment protein droplet morphology, bilateral, grade 1

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* STATE AT NECROPSY: K0
DAYS ON TEST : 7 — * ANIMAL NO. : 9777

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Alpha 2u globulin immunohistological staining, bilateral, grade 2
-altered P2 segment protein droplet morphology, bilateral, grade 1

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT)
INDIVIDUAL ANIMAL DATA

PAGE : 9
PROJECT NO.: DC9620

TEST ARTICLE : HMDS
TEST SYSTEM : RAT (F344), 7 days, inhalation
SPONSOR : dow corning

PATHOL. NO.: 00003 JWC
DATE : 26-JUN-02
PathData® System V6.1a

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 01, controls

MALE

* STATE AT NECROPSY: KO
DAYS ON TEST : 7 * ANIMAL NO. : 9778

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:
Died after anesthesia.
KIDNEYS:
FAILED TO PERFUSE

* MICROSCOPIC FINDINGS

KIDNEYS:
Tissue not present for histologic examination

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) — PAGE : 11
INDIVIDUAL ANIMAL DATA — PROJECT NO.: DC9620

TEST ARTICLE : HMDS — *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation — *DATE* : 26-JUN-02
SPONSOR : dow corning — *PathData® System V6.1a*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, High dose — MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 7 — * ANIMAL NO. : 9779

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Cellular Casts, bilateral, grade 1
-Alpha 2u globulin immunohistological staining, bilateral, grade 4
-altered P2 segment protein droplet morphology, bilateral, grade 4

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* STATE AT NECROPSY: K0
DAYS ON TEST : 7 — * ANIMAL NO. : 9780

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Cellular Casts, bilateral, grade 1
-Alpha 2u globulin immunohistological staining, bilateral, grade 4
-altered P2 segment protein droplet morphology, bilateral, grade 4

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) PAGE : 12
INDIVIDUAL ANIMAL DATA PROJECT NO. : DC9620

TEST ARTICLE : HMDS *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation *DATE* : 26-JUN-02
SPONSOR : dow corning *PathData® System V6.1a*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, High dose MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 7 * ANIMAL NO. : 9781

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Cellular Casts, bilateral, grade 2
-Alpha 2u globulin immunohistological staining, bilateral, grade 4
-altered P2 segment protein droplet morphology, bilateral, grade 4

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* STATE AT NECROPSY: K0
DAYS ON TEST : 7 * ANIMAL NO. : 9782

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Cellular Casts, bilateral, grade 1
-Alpha 2u globulin immunohistological staining, bilateral, grade 4
-altered P2 segment protein droplet morphology, bilateral, grade 4

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) PAGE : 13
INDIVIDUAL ANIMAL DATA PROJECT NO. : DC9620

TEST ARTICLE : HMDS *PATHOL. NO.* : 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation *DATE* : 26-JUN-02
SPONSOR : dow corning *PathData® System V6.1a*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, High dose MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 7 * ANIMAL NO. : 9783

* NECROPSY FINDINGS

NO NECROPSY OBSERVATIONS NOTED.

* MICROSCOPIC FINDINGS

KIDNEYS:
-Cellular Casts, bilateral, grade 1
-Alpha 2u globulin immunohistological staining, bilateral, grade 4
-altered P2 segment protein droplet morphology, bilateral, grade 4

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* STATE AT NECROPSY: K0
DAYS ON TEST : 7 * ANIMAL NO. : 9784

* NECROPSY FINDINGS

KIDNEYS:
FAILED TO PERFUSE
NO OTHER NECROPSY OBSERVATIONS NOTED

* MICROSCOPIC FINDINGS

KIDNEYS:
Tissue not present for histologic examination

APPENDIX 1 (continued)

Individual Animal Reports

PATHOLOGY REPORT (DRAFT) PAGE : 14
INDIVIDUAL ANIMAL DATA PROJECT NO.: DC9620

TEST ARTICLE : HMDS *PATHOL. NO.*: 00003 JWC
TEST SYSTEM : RAT (F344), 7 days, inhalation *DATE* : 26-JUN-02
SPONSOR : dow corning *PathData® System V6.1a*

TEXT OF GROSS AND MICROSCOPIC FINDINGS
DOSE GROUP : 02, High dose MALE

* STATE AT NECROPSY: K0
DAYS ON TEST : 7 * ANIMAL NO. : 9785

* NECROPSY FINDINGS

GENERAL OBSERVATIONS:
Died after anesthesia.
KIDNEYS:
ONLY PARTIAL PERFUSION OF KIDNEYS.

* MICROSCOPIC FINDINGS

KIDNEYS:
Tissue not present for histologic examination

APPENDIX 2

Explanation of Codes and Symbols

PATHOLOGY REPORT (DRAFT)

PAGE : 1
PROJECT NO.: DC9620

TEST ARTICLE : HMDS
TEST SYSTEM : RAT (F344), 7 days, inhalation
SPONSOR : dow corning

PATHOL. NO.: 00003 JWC
DATE : 26-JUN-02
PathData® System V6.1a

EXPLANATION OF CODES AND SYMBOLS

CODES AND SYMBOLS USED AT ANIMAL LEVEL:

M = Male animal
K0 = Terminal sacrifice group

CODES AND SYMBOLS USED AT ORGAN LEVEL:

! = Gross observat.not checked off histologically
0 = Tissue not present for histologic examination
' = Histologic examination not required
+ = Organ examined, findings present

CODES AND SYMBOLS USED AT FINDING LEVEL:

GRADE 1 = Minimal / very few / very small
GRADE 2 = Slight / few / small
GRADE 4 = Marked / many / large